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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,400	07/22/2002	Thomas Hantke	0480/01219	2952

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,400	HANTKE ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-25* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted May 10, 2005 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 2, 4, 6-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741).

3. Andries et al. teaches the HIV inhibiting pyrimidine derivatives herein and the method of using the same for preparing pharmaceutical composition, and for treating HIV infection. See, the abstract, cols 1-10, 17-19. The elected compound herein is a preferred compound disclosed by Andries et al. see, col. 10, lines 14-15. The compounds may be formulated into various conventional dosage forms, such as powders, tablet, capsule with solid carrier and other pharmaceutical excipients. See, particularly, col. 18, line 19 to col. 19, line 25. (Applicants also admitted the compounds are known in the art, citing PCT/EP99/02043, which is equivalent to US 6,197,779, and PCT EP/02044, see page 2 herein)

4. Andries et al. do not teach expressly the particular dosage form herein with PVP or it's copolymer as carrier and polyoxyethylene hydrogenated castor oil and citric acid as additional excipients, or the particular release forms.

5. However, Goertz et al. teach a solid pharmaceutical form wherein polyvinylpyrrolidone or copolymer of vinylpyrrolidone and vinyl acetate or used as carrier, and a solid solution of the active ingredient is formed. See particularly, the abstract, col. 3, lines 3-31, col. 4, lines 11-45, and the claims. There is no particular limitation as to the active ingredients employed therein. The concentration of active ingredients may be in the rage from 0.1 to 95%, with preferred range of 30-70%. 45 to 50% of polymer is used in the particular examples. Other known pharmaceutical excipients may be added accordingly. The forms may be made by extrusion. See, cols. 3-8. Nakamichi et al. teach that solid dispersion or solution is known to be useful for controlling the rate of release of a drug from dosage form or improving the bioavailability of drugs. Nakamichi et al. further teaches that other polymeric material, such as modified cellulose (e.g. hydroxypropylmethylcellulose) are similarly useful (like PVP) as solid carrier, and extrusion is a conventional method for making a solid dispersion or solution form. See, particularly, cols. 1-2, and the claims. Both Sasatani et al. and Takada teaches that polyethylene glycol castor oil ester and citric acid are known pharmaceutical excipients and are particularly known to be useful in solid form wherein Polyvinypyrrolidone is carrier. See, particularly, col. 5, lines 33-63 in Sasatani et al. and the claims in Takada.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form,

wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid.
A person of ordinary skill in the art would have been motivated to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid, because polymeric carrier, such as vinylpyrrolidone polymer or copolymer, are known to produce solid dispersion or solution with a drug which provide controlled release and enhanced bioavailability. Further, the employment of various pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil (surfactants), and citric acid (acids), accordingly is within the skill of artisan. The further employment of other polymers, such as hydroxypropylmethylcellulose, would have been obvious since the modified cellulose is known to be similarly useful as a solid carrier. Furthermore, the optimization of a result effective parameter, e.g., drug releasing profile, or the effective amounts of the drug and the other ingredients therein, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

The employment of a dosage form known to be useful for a particular purpose, in a pharmaceutical package useful for the same purpose is considered within the skill of the artisan. Further, the optimization of a dosage regimen for the administration of a dosage form is considered within the skill of the artisan, absent evidence to the contrary.

Response to the Arguments

Applicants' amendments and remarks submitted May 10, 2005 have been fully considered, but are found unpersuasive.

6. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Andries et al. teach the active ingredients herein are known, and are known to be useful in various pharmaceutical forms. The secondary references show that the particular form, solid dispersion based on PVD as carrier is known and each and every other ingredients herein employed are well-known pharmaceutical excipients. Therefore, making the known ingredient into a particular known pharmaceutical form would have been obvious to one of ordinary skill in the art. it is noted that Goertz et al. merely give examples of pharmaceutical excipients and is by no mean to limit the scope of excipients useful in the composition. Further, even within the examples, there are surfactants, such as wetting agents, stearyl alcohol etc. (see the examples). Further, Nakamichi et al. disclosed the employment of high HLB surfactant in the extruded solid dispersion such as polyoxyetheylenpolyoxypropylene glycol (col. 3, lines 33-35). Therefore, the employment of PEG-n-hydrogenated castor oil, a well known pharmaceutical excipients used in solid dispersion, in the solid dispersion herein would have been obvious to one of ordinary skill in the art.

7. In response to applicant's argument that Sasatani et al. and Takada are nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was

concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the cited references are in the same field of applicant's endeavor, i.e., pharmaceutical art, or more specific, solid dispersion composition. Sasatani et al. and Takada disclosed that PEG-n-hydrogenated castor oil is known to be useful in solid dispersion composition. Considering the cited references as a whole, the claimed invention would have been obvious for reasons discussed above.

8. For reasons discussed above, all the claims have been properly rejected.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617